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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,977	10/04/2005	David Deperthes	KZI-002US	3931
959 7590 05/23/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER GUSSOW, ANNE	
			ART UNIT 1643	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/551,977

Applicant(s)

DEPERTHES ET AL.

Examiner

Anne M. Gussow

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1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-10,12-17,21,23-38 and 41-49 is/are pending in the application.
- 4a) Of the above claim(s) 13-16,21,23-27,31-38 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-10,12,17,28-30,41-47 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 04 October 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/8/06</u> . | 6) <input checked="" type="checkbox"/> Other: <u>sequence alignment</u> |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1, 4-10, 12, 17, 28-30, 41-47, and 49, in the reply filed on November 13, 2006 is acknowledged. The traversal is on the ground(s) that the groups set forth in the restriction requirement differ from the lack of unity groups set forth by the International Searching Authority. This is not found persuasive because in the national stage of an application, the examiner is not bound by the findings of the International Searching Authority. For the reasons set forth in the restriction requirement Groups I-VII are distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 13-16, 21, 23-27, 31-38, and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 13, 2006.

3. The sequence listing filed March 8, 2007 has been entered.

The amendment filed March 8, 2007 has been entered.

Claims 1, 4-10, 12, 17, 28-30, 41-47, and 49 are under examination.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on December 8, 2006 has been fully considered by the examiner and an initialed copy of the IDS is included with this Office Action.

Drawings

5. The drawings are objected to because in Figures 2, 19, and 25-27 the labels in shaded areas of the figures are unclear. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Sheets" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d)(1). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

Specification

6. The abstract of the disclosure is objected to because it contains legal phraseology. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

7. The disclosure is objected to because of the following informalities:

a.) the specification contains typographical errors, for example on page 13 line 34, "Shine Dalgarno" should read "Shine Delgarno".

b.) in figure 2, what is the * at the end of the sequence? The meaning of the symbol should be included in the description of the figure.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 4-10, 12, 17, 28-30, 41-47, and 49 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant fusion peptabody which binds to an epidermal growth factor receptor comprising a specific portion of a cartilage oligomer matrix polypeptide (49 amino acids as shown in figure 2), a specific portion of a hinge region of an immunoglobulin polypeptide (19 amino acids from human IgA, see page 10 lines 1-5 and figure 2), an enhancer sequence, and an epidermal growth factor receptor ligand, does not reasonably provide enablement for a recombinant fusion peptabody comprising just any portion of a cartilage oligomer matrix polypeptide, just any portion of a hinge regions of an immunoglobulin polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a recombinant fusion peptabody, which binds to an epidermal growth factor receptor (EGFR) selected from the group consisting of ErbB-1, ErbB-3, and or ErbB-4, comprising a portion of a cartilage oligomer matrix polypeptide, a peptide enhancer sequence for increasing protein production located at the N terminus of the portion of the cartilage oligomer matrix polypeptide, a portion of a hinge region of an immunoglobulin polypeptide located at the C terminus of the portion of the cartilage oligomer matrix polypeptide, and an epidermal growth factor ligand located at the C terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor, wherein said recombinant fusion peptabody is multimeric, wherein the peptide enhancer sequence is selected from the group consisting of SEQ ID Nos. 5-9, wherein said ligand is selected from an epidermal growth factor polypeptide, a growth blocking peptide, a TFG alpha polypeptide, a plasmocyte spreading peptide, a paralytic peptide, a cardioactive peptide, an amphiregulin

polypeptide, a heparin-binding epidermal growth factor-like polypeptide, a betacellulin polypeptide, a viral EGF-like polypeptide, or fragments or variants thereof.

The specification discloses a recombinant fusion peptabody which binds to an epidermal growth factor receptor, comprising an enhancer, 49 amino acids of human oligomeric matrix polypeptide, 19 amino acids of human IgA as a hinge, and a full length human epidermal growth factor (see figure 2). The specification does not provide any direction or guidance to assist one skilled in the art in the selection of all possible portions of the oligomeric matrix polypeptide or the hinge region nor is there evidence provided that all such fragments would be functional. Further, the as-filed specification fails to address the following issues:

- 1.) would the peptabody comprising any of the ligands claimed bind to an EGFR
- 2.) would the length of the polypeptide portions affect the folding and/or function of the peptabody

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess, et al., 1990. Journal of Cell Biology, Vol. 111 pages 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar, et al., 1988. Molecular and Cellular Biology, Vol. 8 No. 3 pages 1247-1252). Replacement of the histidine at position 10 of the B-

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chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz, et al., 1987. Proc Natl Acad Sci Vol. 84 pages 6408-6411). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin, et al., 1975. Biochemistry, Vol. 14 pages 1559-1563). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting synthetic DNA sequence. The results of the construction of synthetic proteins remain very unpredictable as Burgess, et al., Lazar, et al., Schwartz, et al., and Lin, et al. conclusively demonstrate.

Regarding the enhancer sequences, the instant SEQ ID No. 6 (YSFEDL) is identical to SEQ ID No. 21 of Wickham, et al. (WO 2001/92549, December 6, 2001). Wickham et al. disclose SEQ ID No. 21 to be a ligand for an integrin substrate (see paragraph 13, page 4 and sequence alignment). One of skill in the art would be able to select an enhancer from known enhancer sequences in the art, however, the instant disclosed enhancers are not known as enhancer sequences, rather as a ligand sequence. Additionally, Fattah, et al. (International Journal of Cancer, 2006. Vol. 119, pages 2455-2463) teach that huge variations of the production yield of peptabody-EGF were observed between different enhancers (see top of page 2458).

Regarding the ligands, Fattah, et al. teach peptabody-EGF is specific for cells

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overexpressing EGF in vitro (see figure 5). Additionally, Fattah, et al. teach that fusing a complex protein molecule such as the human epidermal growth factor to the peptabody core represented a big challenge mostly because of various intra- and intermolecular disulfide bridges that had to be formed correctly (page 2460, Discussion).

In view of the lack of predictability of the art to which the invention pertains undue experimentation would be required to produce the claimed peptabody with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively produce the claimed peptabody and absent working examples providing evidence which is reasonably predictive that the broadly claimed peptabody is functional commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 4, 6-10, 17, 44-46, and 49 are rejected under 35 U.S.C. 103(a) as being obvious over Houimel, et al. (International Journal of Cancer, 2001. Vol. 92, pages 748-755, as cited in prior action) in view of Azevedo, et al. (Brazilian Journal of Medical and Biological Research, 1999. Vol. 32, pages 147-153).

The claims recite a recombinant fusion peptabody which binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3, and or ErbB-4, comprising a portion of a cartilage oligomer matrix polypeptide, a peptide enhancer sequence for increasing protein production located at the N terminus of the portion of the cartilage oligomer matrix polypeptide, a portion of a hinge region of an immunoglobulin polypeptide located at the C terminus of the portion of the cartilage oligomer matrix polypeptide, and an epidermal growth factor ligand located at the C

terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor, wherein said recombinant fusion peptabody is multimeric, wherein said ligand is selected from an epidermal growth factor polypeptide, a growth blocking peptide, a TFG alpha polypeptide, a plasmocyte spreading peptide, a paralytic peptide, a cardioactive peptide, an amphiregulin polypeptide, a heparin-binding epidermal growth factor-like polypeptide, a betacellulin polypeptide, a viral EGF-like polypeptide, or fragments or variants thereof, wherein said epidermal growth factor receptor ligand is present in its full-length sequences, wherein the peptabody further comprises a polyhistidine tag sequence, further comprising at least one effector region comprising a cytotoxin or a detection moiety. The claims also recite a pharmaceutical composition comprising the recombinant fusion peptabody of claim1, and a pharmaceutically acceptable carrier.

Houimel, et al. teach a recombinant peptabody comprising peptide sequences that bind to ErbB-2, the coiled-coil assembly domain of the human cartilage oligomeric matrix protein (hCOMP), a hinge region derived from human IgA1, and a his6-tag (page 749). Houimel, et al. do not teach an enhancer sequence. This deficiency is made up for in the teachings of Azevedo, et al.

Azevedo, et al. teach commonly used enhancers in mammalian expression plasmids (page 148).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a recombinant peptabody

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comprising the peptide sequences of Houimel, et al. and the enhancer sequence of Azevedo, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a recombinant peptabody of Houimel, et al. and use an enhancer as taught by Azevedo, et al. because Azevedo, et al. teach enhancers are useful for gene therapy and genetic immunization because of their high transcription initiation ability in mammalian tissues. Additionally, Houimel, et al. teach that ErbB2 is activated through heterodimerization with ErbB1, ErbB3, and ErbB4, therefore, one of skill in the art would envisage that a peptabody which recognized ErbB2 would also recognize the other closely related members of the Erb family. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the enhancer of Azevedo, et al. to increase expression of the peptabody of Houimel, et al.

The intended use of the pharmaceutical composition carries no patentable weight in this rejection and the wherein clause in claim 1 does not add anything, if you have the composition then it would be capable of inducing cellular death.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

14. Claims 1, 4, 6-10, 17, 28-30, 44-46, and 49 are rejected under 35 U.S.C. 103(a) as being obvious over Houimel, et al. (International Journal of Cancer, 2001, *supra*) in

view of Azevedo, et al. (Brazilian Journal of Medical and Biological Research, 1999, supra), and further in view of Goins, et al. (US PG PUB 2002/0164648, November 7, 2002).

Claims 1, 4, 6-10, 44-46, and 49 have been described supra. Claims 17 and 28-30 recite a pharmaceutical composition comprising the recombinant fusion peptabody of claim 1, and a pharmaceutically acceptable carrier; a kit for treating cancer characterized by expression of an epidermal growth factor receptor selected from the group consisting of ErbB1, BrbB3, and ErbB4, in a human patient, said kit comprising the recombinant fusion peptabody of claim 1 and/or instructions for administering the recombinant fusion peptabody to the human patient for the treatment of cancer, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group consisting of a chemotherapeutic agent, an anti-epidermal growth factor receptor antibody, a radioimmunotherapeutic agent, and combinations thereof; a kit for diagnosing cancer characterized by the expression of an epidermal growth factor receptor selected from the group consisting of ErbB1, ErbB3, and ErbB4, in a human patient, comprising the recombinant fusion peptabody of claim 10 and instructions for use.

Houimel, et al. has been described supra.

Azevedo, et al. has been described supra. Houimel, et al. and Azevedo, et al. do not teach a pharmaceutical composition or a kit comprising the recombinant peptabody. This deficiency is made up for in the teachings of Goins, et al.

Goins, et al. teach kits containing a ligand and antibody with a detection or therapeutic agent (see examples 5 and 6).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a recombinant peptabody of Houimel, et al. with the enhancer of Azevedo, et al. in the kit in view of Goins, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a recombinant peptabody of Houimel, et al. with the enhancer of Azevedo, et al. in the kit of Goins, et al. because Goins, et al. teach that peptabodies could substitute for the antibody in the antibody/antigen pair and be used in conjunction with a corresponding molecule (example 4, paragraph 107). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the peptabody of Houimel, et al. and the enhancer of Azevedo, et al. in a kit in view of Goins, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

Conclusion

15. No claims are allowed.


LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

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16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow, Ph.D.

May 17, 2007

<!--StartFragment-->RESULT 4

AAE18001

ID AAE18001 standard; peptide; 9 AA.

XX

AC AAE18001;

XX

DT 07-MAY-2002 (first entry)

XX

DE Human ligand #21 attached to an adenoviral vector.

XX

KW Human; adenoviral coat protein; non-native ligand; cell-surface receptor;
KW therapy; anti-tumour agent; tumour necrosis factor; cancer; brain; lung;
KW ovary; breast; prostate.

XX

OS Homo sapiens.

XX

PN WO200192549-A2.

XX

PD 06-DEC-2001.

XX

PF 30-MAY-2001; 2001WO-US017391.

XX

PR 31-MAY-2000; 2000US-0208451P.

PR 02-AUG-2000; 2000US-00631191.

XX

PA (GENV-) GENVEC INC.

XX

PI Wickham TJ, Kovesdi I, Roelvink PW, Einfeld D, Brough DE;

PI Lizonova A;

XX

DR WPI; 2002-147620/19.

XX

PT Adenoviral coat protein which permits production of adenoviral vectors
PT that bind and infect host cells not naturally infected by adenovirus,
PT comprises various non-native ligands.

XX

PS Claim 4; Page 43; 45pp; English.

XX

CC The invention relates to adenoviral coat proteins comprising various non-
CC native ligands. The invention provides a method of controlled gene
CC expression utilising selectively replication competence and also a method
CC and a composition for targetting an adenoviral vector. A system
CC comprising a cell having a non-native cell-surface receptor, and a virus
CC having a non-native ligand which binds the non-native cell-surface
CC receptor of the cell is useful for propagating a virus and also for
CC assaying gene function. The system is also useful for isolating a nucleic
CC acid encoding a product comprising a desired property. Further the system
CC is useful for identifying functionally related coding sequences.
CC Adenoviral vector comprising a non-native nucleic acid encoding a
CC therapeutic agent such as anti-tumour agent, preferably tumour necrosis
CC factor and a second non-native nucleic acid encoding an agent that
CC facilitates imaging and a targetting agent is useful for treating an
CC animal. The therapeutic agent can be used to treat cancer of the brain,
CC lung, ovary, breast and prostate. The present sequence is human non-
CC native ligand attached to an adenoviral vector

XX

SQ Sequence 9 AA;

Query Match 100.0%; Score 32; DB 5; Length 9;

Best Local Similarity 100.0%; Pred. No. 2.3e+06;

Matches 6; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YSFEDL 6
 | | | | |
Db 1 YSFEDL 6

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